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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,863	10/30/2003	David E. Clapham	110313.135US3	1595

23483 7590 11/12/2010

WILMERHALE/BOSTON
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
11/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

teresa.carvalho@wilmerhale.com
whipusptopairs@wilmerhale.com

Office Action Summary	Application No.	Applicant(s)	
	10/697,863	CLAPHAM ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 8-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 8-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

Claims 1, 3-6 and 8-25 are pending in the instant application. Claims 2, 7 and 26-111 have been cancelled. Claims 1, 3-6 and 8-11 are amended.

Claims 1, 3-6 and 8-25 are under examination in the instant Office Action.

Withdrawn Objections/Rejections

Claim Rejections-35 USC § 112, first paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

The rejection of claims 1, 3-6 and 8-25, under 35 U.S.C. § 112-1st paragraph, for improper breadth based on 80% sequence homology and undefined fragments, is *withdrawn* based on applicant's amendments to independent claims (29 December 2009).

35 USC § 112, first paragraph - Written Description.

The rejection of Claims 1, 3-6, 8, 10 and 11, under 35 U.S.C. § 112, first paragraph- written description- is *withdrawn* based on applicants' amendment of 29 December 2009.

Claim Rejections- 35 USC § 102

The rejection of claims 1, 3 and 8 under 35 U.S.C. 102(b) as being anticipated by Hillier, et al (1997, Accession No. AA416682.1) is *withdrawn* based on applicant's amendment (29 December 2009). This reference should not be confused with a different reference by the same author, newly cited below, and referred to as Hillier, 1997b.

Likewise, the rejection of Claim 10 under 35 U.S.C. 102(b) for being anticipated by Sanger Centre (1998, Science, 282: 2012-2018, Accession No. Z82256.1) is *withdrawn* based on applicant's amendment (29 December 2009).

New Claim Objections and/or Rejections

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, 5 and 6 recite a "functional equivalent" of SEQ ID NO: 2. It is not known what is meant by this phrase or whether it refers to molecules that behave similarly to the fairly typical calcium channel of SEQ ID NO: 2, or if the phrase refers to homologs, analogs or structural equivalents, or something else altogether. The phrase is not defined in the instant Specification. Defining what is meant by both "functional" and "equivalent" would be remedial, as would removing the phrase.

Claim 4 is included in this rejection because it is ultimately dependent from the specifically-mentioned claims without resolving the indefiniteness issue belonging thereto.

35 U.S.C. § 101-Product of Nature/Gene Therapy

The following is a quotation of 35 U.S.C. 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21-25 are rejected under 35 U.S.C. 101 because the claimed invention encompasses non-statutory subject matter. The phrase "A cell" reads on isolated cells, *as well as* cells in the context of a multicellular, transgenic organism and cells intended for gene therapy. The specification teaches that the cell comprising a heterologous Catsper1 gene can be used for gene therapy (p. 20, last paragraph; p. 22, middle of last paragraph), and in fact claim 25

specifically claims cells intended for gene therapy and for the construction of multicellular transgenic animals. The claims embrace said cell becoming integrated into the human being and therefore being an inseparable part of the human itself. The scope of the claims, therefore, encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation "isolated" or "non-human" would be remedial. See 1077 O.G. 24, April 21, 1987.

Claim Rejections - 35 USC § 112, first paragraph - Scope of enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 3-6 and 8-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for "allelic variants," "functional equivalents," or fragments *consisting essentially* of nucleic acids that hybridize to SEQ ID NO: 1 at moderate stringency. "Consisting essentially of" is interpreted as open language, encompassing unspecified lengths of the claimed nucleic acids or encoded polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 3-6 and 8-25 are drawn to large nucleic acid sequences comprising SEQ ID NO: 1, as well as polynucleotide probes of SEQ ID NO: 1. Experiments were described in the specification which demonstrate that the polypeptide encoded by SEQ ID NO: 1 is a sperm Ca^{2+}

channel necessary for sperm motility (see Figure 4, for example). However, no "allelic variants," "functional equivalents," or fragments *consisting essentially* of SEQ ID NO: 1 or 2 were tested in functional assays.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A sufficient amount of direction or guidance is lacking in claims 3-6 and 8-25. Nowhere in the specification is a functional isoform or variant, or functional fragment of SEQ ID NO: 1 described. It is not known if a significant number of the polynucleotides described in the claims could be expected to behave like a Catsper1 channel, or even whether they would bind as a probe to the claimed nucleic acids. In terms of allelic variants and functional equivalents of the claimed nucleic acids, applicants have not identified any allelic variants of Catsper1 nor any functional equivalents of Catsper1, nor has the literature contributed information concerning isoforms of Catsper1.

Due to the large quantity of experimentation required to: determine how to make a variant or functional fragment of SEQ ID NO: 1 or to isolate an allelic variant of SEQ ID NO: 1; the lack of direction or guidance in the specification regarding same (e.g., the lack of guidance regarding the residues needed to produce a functioning Catsper1 protein from a nucleic acid that "consists essentially" of a sequence that hybridizes to SEQ ID NO: 1); the lack of working

examples in which variants of Catsper1 were made and tested in functional assays, and the state of the art which is silent as to functional equivalents or allelic variants of SEQ ID NO: 1-- undue experimentation would be required of the skilled artisan to make and use the claimed invention.

Applicants contend (Remarks, 29 December 2010, p. 9):

"In various claims, these amendments replace "having" with "consisting essentially of," provide limitations on what constitutes a CatSperl protein, replace 80% identity with 95% identity, and require CatSper1 activity. One of ordinary skill in the art can make and use the subject matter of the amended claims without undue experimentation, based on the instant disclosure."

Applicant's remarks concerning the claim amendments have been fully considered but they are not persuasive for the following reasons:

In terms of the phrase "consisting essentially of," applicant is reminded that, when discussing claims to products rather than method steps, "consisting essentially of" is interpreted similarly to "comprising" (see MPEP § 2111.03), with the added requirement that anything added to the product, in this case the claimed nucleic acids, would not change the "basic and novel characteristic(s)" of the claimed invention" (MPEP § 2111.03, paragraph 3). Since there was no reduction to practice to make variants of SEQ ID NO: 1 and test them to determine if their characteristics have changed from that of a Catsper1 channel, applicants are not enabled for variants of the claimed nucleic acids.

35 USC § 112, first paragraph - Written Description.

Claims 3-6 and 8-25 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-6 and 8-25 are directed to "allelic variants," "functional equivalents," or fragments *consisting essentially* of nucleic acids that hybridize to SEQ ID NO: 1 at moderate stringency. The specification teaches the Catsper1 nucleic acid and polypeptide. However, the specification does not teach functional or structural characteristics of all or a significant number of the nucleic acids encompassed by the claims. The description of one Catsper1 polynucleotide and a polypeptide which is a Catsper1 Ca^{2+} channel is not adequate written description of an entire genus of functionally-equivalent polynucleotides or polypeptides.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of "allelic variants," "functional equivalents," or fragments *consisting essentially* of nucleic acids that hybridize to SEQ ID NO: 1 at moderate stringency. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides; therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making a Catsper1 isoform. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polynucleotide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 (BPAI 1993). In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides comprising the nucleotide sequence set forth in SEQ ID NO: 1, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant's comment about the claim amendments (Remarks, 29 December 2010, bottom of p. 9):

"Applicants have amended claims 1, 3-6, and 8, 10, and 11. In various claims, these amendments replace "having" with "consisting essentially of," provide limitations on what constitutes a

CatSperl protein, replace 80% identity with 95%"

Applicant's remarks concerning the claim amendments have been fully considered but they are not persuasive for the following reasons:

Although allelic variants of SEQ ID NO: 1 and functional equivalents of SEQ ID NO: 1 are mentioned in the instant specification, applicants have not put into practice methods of defining and isolating portions of the Catsper1 channel to determine which variants and equivalents of SEQ ID NO: 1 function like a Catsper1 channel. As such, applicants *were not in possession* of a sufficient number of nucleic acids and polypeptides that would define and constitute a genus of variants and equivalents of SEQ ID NO: 1. In addition, in terms of the added phrase "consisting essentially of," applicant is reminded that, when discussing claims to products rather than method steps, "consisting essentially of" is interpreted similarly to "comprising" (see MPEP § 2111.03). As discussed above, if there was no reduction to practice to make variants of SEQ ID NO: 1 and test them, then applicants were not in possession of any of the claimed nucleic acids, save SEQ ID NO: 1 itself.

Claim Rejections- 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier, et al (1997b, Accession No. AA416577.1). Hillier discloses residues 1959 to 2343 of instant SEQ ID NO: 1 (see the alignment in Appendix A, below). This covers residues 2057 to 2343 of claim 1, as well as the required 10-18 consecutive nucleotides. The nucleic acid disclosed by Hillier also reads on transmembrane domains S3-S6, as recited in claims 3 and 5 (see instant Figure 1(a)), and encodes polypeptides that make up the latter 72% of the Catsper1 channel, encompassing more residues than those listed in the alternative in sections (b)-(c) of claim 4. The sequence disclosed by Hillier also would be expected to hybridize to at least 10 consecutive nucleotides of SEQ ID NO: 1, as required by claim 8.

Conclusion: Claims 1, 3-6 and 8-25 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Nickol, can be reached at (571) 272-0835.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private

PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

/SLW/
31 October 2010

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1646

Appendix A. Search Results

Hillier, 1997b:

```
RESULT 13
AA416577/c
LOCUS       AA416577                 528 bp    mRNA    linear   EST 09-NOV-1997
DEFINITION  zu18d02.s1 Soares_NbHMPu_S1 Homo sapiens cDNA clone IMAGE:738339
            3', mRNA sequence.
ACCESSION   AA416577
VERSION     AA416577.1  GI:2077556
KEYWORDS    EST.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 528)
  AUTHORS   Hillier,L., Allen,M., Bowles,L., Dubuque,T., Geisel,G., Jost,S.,
            Krizman,D., Kucaba,T., Lacy,M., Le,N., Lennon,G., Marra,M.,
            Martin,J., Moore,B., Schellenberg,K., Steptoe,M., Tan,F.,
            Theising,B., White,Y., Wylie,T., Waterston,R. and Wilson,R.
  TITLE     WashU-NCI human EST Project
  JOURNAL   Unpublished (1997)
COMMENT     Contact: Wilson RK
            Washington University School of Medicine
            4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
            Tel: 314 286 1800
            Fax: 314 286 1810
            Email: est@watson.wustl.edu
            This clone is available royalty-free through LLNL ; contact the
            IMAGE Consortium (info@image.llnl.gov) for further information.
            Insert Length: 956  Std Error: 0.00
            Seq primer: -41m13 fwd. ET from Amersham
            High quality sequence stop: 463.
FEATURES             Location/Qualifiers
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                     /mol_type="mRNA"
                     /db_xref="GDB:5945946"
                     /db_xref="taxon:9606"
                     /clone="IMAGE:738339"
                     /tissue_type="Pooled human melanocyte, fetal heart, and
                     pregnant uterus"
                     /lab_host="DH10B"
                     /clone_lib="Soares_NbHMPu_S1"
                     /note="Organ: mixed (see below); Vector: pT7T3D-PacI;
                     Site_1: Not I; Site_2: Sco RI; Equal amounts of plasmid
                     DNA from three normalized libraries (melanocyte 2NbHM,
                     pregnant uterus NbHPU, and fetal heart NbHH19W) were
                     mixed, and as circles were made in vitro. Following HAP
                     purification, this DNA was used as tracer in a subtractive
                     hybridization reaction. The driver was PCR-amplified cDNAs
                     from pools of 5,000 clones made from the same 3 libraries.
                     The pools consisted of I.M.A.G.E. clones 260232-265223,
                     340488-345479, and 484488-489479."
ORIGIN

  Query Match             16.4%;  Score 385;  DB 1;  Length 528;
  Best Local Similarity   100.0%;
  Matches  385;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1959 TTACATCATCATCCAGTACTTCATCTTCCTCAACCTGGTGATTACTGTCCTGGTGGATAG 2018
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        528 TTACATCATCATCCAGTACTTCATCTTCCTCAACCTGGTGATTACTGTCCTGGTGGATAG 469

Qy       2019 CTTCCAGACGGCGCTGTTCAAAGGCTTGAGAAAGCGAAGCAGGAGAGGGCCGCCCGGAT 2078
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        468 CTTCCAGACGGCGCTGTTCAAAGGCTTGAGAAAGCGAAGCAGGAGAGGGCCGCCCGGAT 409

Qy       2079 CCAAGAGAAGCTGCTGGAAGACTCACTGACGGAGCTCAGAGCTGCAGAGCCCAAAGAGGT 2138
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        408 CCAAGAGAAGCTGCTGGAAGACTCACTGACGGAGCTCAGAGCTGCAGAGCCCAAAGAGGT 349

Qy       2139 GGCGAGTGAAGGCACCATGCTGAAGCGGCTCATCGAGAAAAAGTTTGGGACCATGACTGA 2198
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        348 GGCGAGTGAAGGCACCATGCTGAAGCGGCTCATCGAGAAAAAGTTTGGGACCATGACTGA 289
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Qy       2199 GAAGCAGCAGGAGCTCCTGTTCCATTACCTGCAGCTGGTGGCAAGCGTGGAGCAGGAGCA 2258
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        288 GAAGCAGCAGGAGCTCCTGTTCCATTACCTGCAGCTGGTGGCAAGCGTGGAGCAGGAGCA 229

Qy       2259 GCAGAAGTTCCGCTCCCAGGCAGCCGTCATCGATGAGATTGTGGACACCACATTTGAGGC 2318
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        228 GCAGAAGTTCCGCTCCCAGGCAGCCGTCATCGATGAGATTGTGGACACCACATTTGAGGC 169

Qy       2319 TGGAGAAGAGGACTTCAGGAATTGA 2343
              |||||||||||||||||||||||||
Db        168 TGGAGAAGAGGACTTCAGGAATTGA 144
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